

Practitioner's Docket No. MPI98-149P1USRCEM

09/775,803

## IN THE CLAIMS:

Please amend claims 1, 5, 10, 15, 21, 23, and 26-30.

No new matter has been added.

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A transgenic mouse comprising a modified glycoprotein V (GP V) gene, wherein at least one allele of said gene has been modified ~~so that the mouse does not express a functional GP V protein or expresses a GPV protein which demonstrates a reduced functionality as compared with the native or wild type GP V protein by a construct which removes a sequence of GP V comprising nucleotides encoding Met 1 to Leu 389 of SEQ ID NO:12~~ and wherein said mouse has a decreased bleeding time compared to a mouse homozygous for the wild type GP V gene.

2. (canceled)

3. (Previously presented) Platelets isolated from blood plasma of the mouse of claim 1.

4. (canceled)

5. (Currently amended) A method of preparing a transgenic mouse comprising a modified glycoprotein V gene, wherein at least one allele of said gene has been modified ~~so that the mouse does not express a functional GP V protein or expresses a GPV protein which demonstrates a reduced functionality as compared with the native or wild type GP V protein by a construct which removes a sequence of GP V comprising nucleotides encoding Met 1 to Leu 389 of SEQ ID NO:12~~ and wherein said mouse has a decreased bleeding time, said method comprising:

- a) introducing into embryonic stem cells a nucleic acid molecule encoding a modified GP V gene; and
- b) generating a transgenic mouse from the cells resulting from step a); and
- c) determining that the bleeding time of the transgenic mouse is less than the bleeding time of a mouse homozygous for the GP V gene.

6. (canceled)

7. (canceled)

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8. (Previously presented) The method of claim 5 further comprising the step of breeding the transgenic mouse so as to produce a mouse homozygotic for the modified GP V gene.

9. (canceled)

10. (Currently amended) A method of preparing a transgenic mouse comprising a nonfunctional glycoprotein V gene, wherein at least one allele of said gene has been modified ~~so that the mouse does not express a functional GP V protein or expresses a GPV protein which demonstrates a reduced functionality as compared with the native or wild type GP V protein by a construct which removes a sequence of GP V comprising nucleotides encoding Met 1 to Leu 389 of SEQ ID NO:12 and wherein said mouse has a decreased bleeding time~~, said method comprising:

- a) introducing into embryonic stem cells a nucleic acid molecule encoding a disrupted or nonfunctional GP V gene and a selectable marker;
- b) identifying and selecting transformed cells;
- c) injecting the transformed cells from step b) into blastocysts; and,
- d) generating a transgenic mouse from the blastocysts of step c), wherein the generated transgenic mouse is chimeric for the disrupted or nonfunctional GP V gene and wherein said mouse has a decreased bleeding time compared to a mouse homozygous for the wild type GP V gene.

11. (canceled)

12. (canceled)

13. (Previously presented) The method of claim 10 further comprising the following steps:

- e) breeding the chimeric mouse with a wild-type mouse to produce a mouse heterozygotic for the nonfunctional GP V gene;
- f) crossing a heterozygotic mouse produced in step e) with a chimeric mouse or a heterozygotic mouse; and,
- g) selecting a mouse homozygotic for the nonfunctional GP V gene from the resulting progeny.

14. (canceled)

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15. (Currently amended) A method to identify an agent that modulates a thrombotic response of a transgenic mouse having a modified GP V gene, wherein at least one allele of ~~so that the mouse does not express a functional GP V protein or expresses a GPV protein which demonstrates a reduced functionality as compared with the native or wild type GP V protein by a construct which removes a sequence of GP V comprising nucleotides encoding Met 1 to Leu 389 of SEQ ID NO:12~~ and wherein said mouse has a decreased bleeding time compared to a mouse homozygous for the wild type GP V gene, comprising the step of exposing the mouse to the agent and determining whether the agent modulates the thrombotic response.

16 - 20 (canceled)

21. (Currently amended) A method of determining the effect of an agent on a characteristic of a mouse that is attributable to the expression of the GP V gene, wherein at least one allele of ~~so that the mouse does not express a functional GP V protein or expresses a GPV protein which demonstrates a reduced functionality as compared with the native or wild type GP V protein by a construct which removes a sequence of GP V comprising nucleotides encoding Met 1 to Leu 389 of SEQ ID NO:12~~ and wherein said mouse has a decreased bleeding time compared to a mouse homozygous for the wild type GP V gene, and wherein said characteristic is platelet function, said method comprising;

- a) administering said agent to the mouse of claim 1;
- b) maintaining said mouse for a desired period of time after said administration; and,
- c) determining whether the characteristic of said mouse that is attributable to the expression of the modified GP V gene has been affected by the administration of said agent.

22. (canceled)

23. (Currently amended) A cell line isolated from a transgenic mouse that comprises a transgene stably integrated into the mouse's genome, said transgene encoding a modified glycoprotein V gene, wherein at least one allele of ~~so that the mouse does not express a functional GP V protein or expresses a GPV protein which~~ said gene has been modified

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~~demonstrates a reduced functionality as compared with the native or wild type GP V protein by a construct which removes a sequence of GP V comprising nucleotides encoding Met 1 to Leu 389 of SEQ ID NO:12 and wherein said mouse has a decreased bleeding time compared to a mouse homozygous for the wild type GP V gene.~~

24. (Currently amended) The cell line of claim 23, wherein said transgene has been introduced into said mouse or an ancestor of said mouse via homologous recombination in embryonic stem cells, and further wherein said mouse expresses a modified GP V protein.

25. (canceled)

26. (Currently amended) The cell line of claim 24, wherein said mouse is fertile and transmits the modified GP V gene to its offspring.

27. (Currently amended) The cell line of claim 23, wherein the modified GP V protein is nonfunctional.

28. (Currently amended) A method of determining the effect of an agent on a characteristic of a mouse that is attributable to the expression of the GP V gene, wherein at least one allele of said gene has been modified so that the mouse does not express a functional GP V protein or expresses a GPV protein which demonstrates a reduced functionality as compared with the native or wild type GP V protein by a construct which removes a sequence of GP V comprising nucleotides encoding Met 1 to Leu 389 of SEQ ID NO:12 and wherein said mouse has a decreased bleeding time compared to a mouse homozygous for the wild type GP V gene, and wherein said characteristic is hemostasis, said method comprising:

- a) administering said agent to the mouse of claim 1;
- b) maintaining said mouse for a desired period of time after said administration; and,
- c) determining whether the characteristic of said mouse that is attributable to the expression of the modified GP V gene has been affected by the administration of said agent.

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29. (Currently amended) A method of determining the effect of an agent on a characteristic of a mouse that is attributable to the expression of the GP V gene, wherein at least one allele of said gene has been modified ~~so that the mouse does not express a functional GP V protein or expresses a GPV protein which demonstrates a reduced functionality as compared with the native or wild type GP V protein by a construct which removes a sequence of GP V comprising nucleotides encoding Met 1 to Leu 389 of SEQ ID NO:12~~ and wherein said mouse has a decreased bleeding time compared to a mouse homozygous for the wild type GP V gene, and wherein said characteristic is coagulation, said method comprising;

- a) administering said agent to the mouse of claim 1;
- b) maintaining said mouse for a desired period of time after said administration; and,
- c) determining whether the characteristic of said mouse that is attributable to the expression of the modified GP V gene has been affected by the administration of said agent.

30. (Currently amended) A method of determining the effect of an agent on a characteristic of a mouse that is attributable to the expression of the GP V gene, wherein at least one allele of said gene has been modified ~~so that the mouse does not express a functional GP V protein or expresses a GPV protein which demonstrates a reduced functionality as compared with the native or wild type GP V protein by a construct which removes a sequence of GP V comprising nucleotides encoding Met 1 to Leu 389 of SEQ ID NO:12~~ and wherein said mouse has a decreased bleeding time compared to a mouse homozygous for the wild type GP V gene, and wherein said characteristic is thrombosis, said method comprising;

- a) administering said agent to the mouse of claim 1;
- b) maintaining said mouse for a desired period of time after said administration; and,
- c) determining whether the characteristic of said mouse that is attributable to the expression of the modified GP V gene has been affected by the administration of said agent.

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